

**REMARKS**

This Amendment is responsive to the Office Action mailed October 17, 2008. With this submission, claim 2 has been amended, claim 6 has been cancelled, and claim 8 has been added. Claims 1-5 and 7-8 are pending; claims 3-5 and 7 are under consideration; and claims 1-2 are withdrawn, subject to rejoinder at the Examiner's discretion. Applicants submit that new claim 8 is examinable with the elected subject matter.

Support for the instant amendment can be found throughout the specification as filed, e.g., at page 11, first full paragraph through page 13, first full paragraph. Reconsideration and withdrawal of the rejections made in the above-referenced Office Action are respectfully requested in view of the following remarks.

**Requirement for Restriction**

The Office has considered Applicants' traversal of the Requirement for Restriction mailed June 17, 2008, but has deemed Applicants' arguments unpersuasive because Applicants have not provided a certified translation of the Japanese priority document to antedate the Nakatsura document. Accordingly, the Office has made the Requirement for Restriction final.

In response, Applicants hereby submit a verified translation of Japanese foreign priority document JP 2003-368725, filed October 29, 2003. Applicants respectfully request that the Examiner review the priority document to ascertain its impact on the Requirement for Restriction.

**Information Disclosure Statement**

Applicants thank the Examiner for acknowledgement of receipt of the Information Disclosure Statements filed November 13, 2007 and November 30, 2007.

Applicants further submit that the attached Information Disclosure Statement lists the previously stricken abstracts for Japanese language documents and indicates both the source and the date of the translation.

Applicants also respectfully note again that the publication date of the Nakatsura et al. document, made of record on the Form PTO-892 mailed on June 17, 2008 is incorrect. The publication date of the Nakatsura document (*Clinical Cancer Research* Vol. 10: pages 6612-6621) is October 1, 2004 – and not October 1, 2003 – as listed on the PTO-892.

Claim Rejections – 35 U.S.C. § 101

The Office Action rejects claim 6 under 35 U.S.C. § 101 as allegedly reciting a use without setting forth any steps involved in the process, resulting in an allegedly improper process claim.

In response, Applicants submit that the present Amendment is fully responsive to the instant rejection set forth under 35 U.S.C. § 101.

Claim Rejections – 35 U.S.C. § 102(a)

The Office Action rejects claims 3-7 under 35 U.S.C. § 102(a) as allegedly anticipated by Nakatsura *et al.* (*Clinical Cancer Research* Vol. 10: pages 6612-6621, October 1, 2004; hereinafter NAKATSURA).

In response, Applicants hereby submit a verified translation of Japanese foreign priority document JP 2003-368725, filed October 29, 2003. Applicants respectfully request that the Examiner review the priority document to ascertain its impact on the outstanding art-based rejections, including the instant rejection under 35 U.S.C. § 102(a).

Claim Rejections – 35 U.S.C. § 103(a)

The Office Action rejects claims 3-7 under 35 U.S.C. § 103(a) as allegedly unpatentable over Katagiri *et al.* (U.S. 2003/0165954 A1; published September 4, 2003; hereinafter KATAGIRI) in view of Desai *et al.* (*J. Med. Genet.* **35**:476-481 (1998); hereinafter DESAI) as evidenced by NAKATSURA. In particular, the Office Action states that KATAGIRI teaches detecting the level of expression of one or more drug sensitivity genes such as GPC3 comprising detecting the level of mRNA with a nucleic acid probe or detecting the level of polypeptide with an antibody specific to the polypeptide.

The Office Action also states that KATAGIRI does not disclose that GPC3 expression is associated with skin cancers such as melanoma (see page 8, lines 4-8 of the Office Action mailed October 17, 2008). For this missing feature, the Office relies upon DESAI as evidenced by NAKATSURA, which allegedly teach that “GPC3 [sic] may be related to a class of skin-related disorders” and that GPC3 expression is an inherent characteristic of melanoma.

The Office Action further asserts that one of ordinary skill in the art would have been motivated to combine the teachings of KATAGIRI and DESAI as evidenced by NAKATSURA because “Katagiri and Desai teach expression of GCP3 [sic] in hyperproliferative disorders and cancer” and because Desai allegedly “provides motivation to consider GCP3 [sic] expression as being correlative for disorders falling within juvenile polyposis which present with dermatological abnormalities including skin cancers and increased numbers of pigmented nevi” (see the Office Action at the bottom half of page 10).

In response, Applicants submit that the claimed subject matter is not unpatentable over KATAGIRI in view of DESAI as evidenced by NAKATSURA. In particular, Applicants submit that KATAGIRI and DESAI, either alone or in combination, do not disclose or suggest the

instant invention. Furthermore, NAKATSURA does not compensate for the deficiencies of the KATAGIRI and DESAI documents.

First, KATAGIRI is silent with respect to the use of GPC3 expression detection for malignant melanoma. Indeed, KATAGIRI makes no mention of the detection or diagnosis of skin cancers or melanoma at all.

Second, DESAI discloses phenotypic features in juvenile polyposis (JP). DESAI, like KATAGIRI, is silent with regard to the use of GPC3 expression detection for malignant melanoma. Instead, DESAI discloses that one patient with JP was also found to have “many of the features” of Simpson-Golabi-Behmel (SGB) syndrome, a known X linked condition of variable mental handicap with overgrowth, macrocephaly, hypertelorism, polydactyly, rib abnormalities, and occasionally cleft palate (page 479, 2<sup>nd</sup> column, first paragraph). DESAI further discloses that tests for germline mutations in the PGC3 gene – not detection of GPC3 expression – should allow for the detection of SGB – not JP or melanoma – in the cohort studied (page 479, 2<sup>nd</sup> column, first paragraph). Thus, KATAGIRI and DESAI, either alone or in combination, fail to teach the claimed invention.

Furthermore, NAKATSURA does not compensate for the deficiencies of the KATAGIRI and DESAI documents. NAKATASURA teaches GPC3 expression in malignant melanoma, and neither KATAGIRI nor DESAI make any mention, much less disclose GPC3 expression as it relates to malignant melanoma. Thus, the NAKATSURA document does not support the Office’s rejection of claims as obvious over KATAGIRI in view of DESAI.

Moreover, Applicants submit that any motivation to combine the cited documents as set forth by the Examiner is accordingly moot in view of the failure of these documents to teach the claimed invention. However, even if *arguendo*, the Office finds that the motivation to combined

the cited documents is not moot, Applicants submit that KATAGIRI and DESAI do not teach expression of GPC3 in hyperproliferative disorders and cancer as the Office asserts. As stated previously, DESAI teaches tests for germline mutations in the PGC3 gene – not detection of GPC3 expression. Furthermore, DESAI teaches PGC3 mutation detection for confirmation of SGB syndrome, not for detection of JP or melanoma. Therefore, DESAI does not provide motivation to consider GPC3 expression as being correlative for disorders falling within juvenile polyposis which present with dermatological abnormalities including skin cancers and increased numbers of pigmented nevi. At best DESAI provides motivation to test patients with JP for germline mutations in the GPC3 gene in order to determine whether these patients also have SGB syndrome.

Finally, Applicants respectfully request that the Examiner review the verified translation of Japanese foreign priority document JP 2003-368725, filed October 29, 2003 to ascertain its impact on the outstanding rejection. Applicants further submit that to the extent that the rejection relies on NAKATSURA, its removal as prior art by submission of the translated priority document herewith renders moot the entire rejection.

For at least the foregoing reasons, Applicants submit that KATAGIRI, DESAI and NAKATSURA, either alone or in combination, do not disclose or suggest the instant invention, and respectfully request withdrawal of the rejection under 35 U.S.C. § 103.


### CONCLUSION

In view of the foregoing remarks and amendments, Applicants respectfully submit that the claims are in condition for allowance.

Inasmuch as the Office Action sets a three-month shortened statutory period for response, to end January 19, 2009 (January 17, 2009 falling on a Saturday), no fee is believed necessary. However, the Office is authorized to charge any required fee to Deposit Account No. 19-0089.

If there should be any questions, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully Submitted,  
Yasuharu Nishimura et al.

  
Bruce H. Bernstein  
Reg. No. 29,027      42,920

January 6, 2009  
GREENBLUM & BERNSTEIN, P.L.C.  
1950 Roland Clarke Place  
Reston, VA 20191  
(703) 716-1191